1: Biotechniques. 1992 Sep;13(3):412-21. Related Articles, Links

The use of synthetic peptide combinatorial libraries for the identification of bioactive peptides.

Houghten RA, Appel JR, Blondelle SE, Cuervo JH, Dooley CT, Pinilla C.

Torrey Pines Institute for Molecular Studies, San Diego, CA 92121.

The systematic preparation of synthetic peptide combinatorial libraries (SPCLs), each composed of tens of millions of peptides that can be screened in existing diagnostically or pharmacologically relevant in vitro assay systems, is reviewed. The identification of optimal peptide sequences has been achieved through the screening in solution of SPCLs, each element of which is composed of more than 100,000 nonsupport-bound peptides in equimolar representation, along with an iterative synthesis and screening process. Examples are presented in which an SPCL, composed in total of 52,128,400 acetylated hexa-peptides, is used along with an iterative selection process to precisely identify the antigenic determinant of a peptide recognized by a monoclonal antibody using competitive enzyme-linked immunosorbent assay. This same library was also used to develop highly potent antimicrobial peptides in bacterial growth inhibition assays. A separate non-acetylated SPCL was used to screen and identify high affinity peptide ligands using an opiate radio-receptor binding assay.

PMID: 1382470 [PubMed - indexed for MEDLINE]

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1: Anticancer Drug Des. 1997 Apr;12(3):145-67. Related Articles, Links

Application of combinatorial library methods in cancer research and drug discovery.

Lam KS.

Arizona Cancer Center, University of Arizona College of Medicine, Tucson 85724, USA.

Combinatorial chemistry is now considered as one of the most important recent advances in medicinal chemistry. There are five general approaches in combinatorial peptide library methods: biological libraries; spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the 'one-bead one-compound' library method; and synthetic library methods using affinity chromatography selection. Except for the biological library approach, which is limited to peptide libraries with eukaryotic amino acids, all the other four synthetic approaches are applicable to peptide, non-peptide oligomer or small molecule libraries. Although non-peptide or small molecule libraries are generally prepared by a synthetic approach, recent advances in biosynthetic methods using enzymes may enable one to prepare chemical libraries that are otherwise difficult to synthesize chemically. In the 'one-bead one-compound' library method every member of the library is screened in parallel, but the chemical structure of the positive compound-bead has to be determined either directly or via an encoding strategy. A reliable high-throughput biological assay is needed for a successful combinatorial library screen. Solid-phase binding or functional assays as well as solution phase assays have been used successfully in various library methods. There has been enormous progress in the technological advances of molecular biology and the fundamental understanding of the molecular basis of cancer in recent years. By applying combinatorial chemistry and computational chemistry to the many cancer targets that have recently been identified, it is hopeful that more potent, more specific and less toxic anti-cancer agents will be developed in the foreseeable future. In addition to being a great tool for drug discovery, combinatorial chemistry has also proven to be invaluable in basic research. A few specific examples of the applications of combinatorial chemistry in basic cancer research and drug discovery are described in this mini-review.

Publication Types:
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